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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,267	08/22/2003	Kathryn Lindsay Ball	CCI-007USDV	9453
959	7590	07/23/2007		
LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER LUKTON, DAVID	
			ART UNIT 1654	PAPER NUMBER
			MAIL DATE 07/23/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<p align="center"><b>Office Action Summary</b></p>	<p><b>Application No.</b></p> <p>10/646,267</p>	<p><b>Applicant(s)</b></p> <p>BALL ET AL.</p>	
	<p><b>Examiner</b></p> <p>David Lukton</p>	<p><b>Art Unit</b></p> <p>1654</p>	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 April 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8 and 11-13 is/are pending in the application.
- 4a) Of the above claim(s) 6,7 and 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5,8,11 and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

Pursuant to the directives of the response filed 4/25/07, claim 1 has been amended. Claims 1-8, 11-13 remain pending.

Claims 1-5, 8, 11, 12 are examined in this Office action; claims 6, 7 and 13 are withdrawn from consideration, as these claims do not encompass the elected species.

Applicants have argued that if a restriction is imposed between a "first" peptide and a "second" peptide, wherein the "first" peptide is a subsequence of the "second" peptide, and if the "first" peptide is determined to be novel, the examiner is then obligated to rejoin claims to the "second" peptide. However, there is no authority or basis for such an assertion. It is entirely possible, and often is the case, that a "first" peptide subsequence will be novel, even as the second peptide (which contains the first peptide) is not novel. Accordingly, claims will not be rejoined if they permit the "carrier" or "partner" to be a peptide.



The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As applicants have argued, Harper, (*Mol Biol Cell* 6, 387-400, 1995) discloses (at page 391) that all fragments of p21 are inactive in any assay which can be used to determine inhibition of a G1 cdk.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

Accordingly, "undue experimentation" would be required to practice the claimed invention.



The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §102(a) as being anticipated by Ball (*Current Biology* 7, 71-80, 1996).

Ball discloses the invention substantially as claimed.

Applicants have asserted that they enjoy an effective file date of 5/8/96, as all instantly claimed embodiments were disclosed in UK 9609521.1. Applicants, however, are not correct. It is noted that UK 9609521.1 and UK 9621314.5 disclose that a peptide which consists of residues 46-65 of p21<sup>WAF1</sup> or residues 16-35 or p21<sup>WAF1</sup> will "inhibit cdk4". However, there does not appear to be descriptive support for "a peptide fragment of 40 amino acids or less", or "a peptide fragment of 40 amino acids or less" which contains the sequence KxxRRyFzP. Nor does there appear to be descriptive support for a method of inhibiting any activity of any G1 cdk.

If applicants want to retain the full benefit of a priority claim to 5/8/96, it is suggested that applicants recite the language that is used in UK 9609521.1.

✦

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the

invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §103 as being unpatentable over Nakanishi (*EMBO Journal* 14(3), 555-63, 1995).

As indicated previously, Nakanishi discloses (page 560, col 2) that peptides containing the following sequence inhibit cyclin-dependent kinases:

WMNFDFXXXXPLEGXXXWXXV

As before, the issue remains that instant claim 1 does not actually require that the peptide in question contain the subsequence RRYFz. In traversing, applicants have noted the examiner's previous argument and have asserted that claim 1 as amended precludes the possibility that the derivative of the peptide fragment can be a peptide which does not contain the sequence KxxRRyFzP. However, applicants are not correct. Claim 1 recites the following:

"wherein the peptide fragment of (i) or the derivative of (ii) comprises ... KxxRRyFzP"

Because of the conjunction "or", as used in claim 1, the claim has effectively eliminated any requirement that the "substance" contain the recited "motif" at all. That is, for the examiner who is endeavoring to reject option (i) in claim 1, he can relegate the requirement for the motif (to be present) to option (ii); conversely, in rejecting option (ii) in claim 1, he can relegate the requirement for the motif (to be present) to option (i). [Furthermore, claim 3 does not require any of the limitations of claim 1, and so no amendment of claim 1 will overcome this rejection as it applies to claim 3]. And if applicants were to amend claim 1 to clearly and unambiguously require both (i) and (ii) to contain the recited motif, this would still leave options (iii), (iv), (v) and (vi) open to interpretation. By contrast, consider the following phrase:

wherein the peptide fragment of (i), (iii) and (v) and the derivative of (ii), (iv) and (vi) **each** comprises the motif KxxRRyFzP

This phrase would leave little room for interpreting claim 1 as is now justified.

But given the claims as rendered, justification exists for maintaining the rejection.



Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §103 as being unpatentable over Chen, J. (*Molecular & Cellular Biology* 16(9) 4673-4682, 1996).

Chen discloses (page 4674, col 1, paragraph 10) the following peptide:

ACRRLFGPVDSE

Chen also discloses that this, and other peptides inhibit cyclin dependent kinases.

Thus, the claims are rendered obvious.

In response, applicants have argued that they enjoy an effective file date of 5/8/96, as all instantly claimed embodiments were disclosed in UK 9609521.1. However, as explained above, (the §102 over Ball), applicants are not correct. The rejection is maintained.



Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §103 as being unpatentable over (a) Xiong Y (*Nature* **366**(6456), 701-4, 1993) or (b) Harper, (*Mol Biol Cell* **6**, 387-400, 1995) in view of Xiong.

Xiong and Harper both teach that p21 inhibits cyclin dependent kinases; Xiong provides the sequence of p21.

Certainly, the teachings of Harper and Xiong taken together disclose a method of inhibiting the activity of a G1 cdk by contacting the cdk with a peptide that comprises (a) a fragment of less than 40 amino acids of p21 and (b) a "carrier" peptide, which happens to be another portion of p21. This conclusion is also reached by considering Xiong by itself. As it happens, however, this particular embodiment is excluded by the claims. But what is not excluded is "non-p21 peptide sequences" that are rendered obvious by Xiong. Consider the following peptide, which is a fragment of p21 (in p21, this happens to be bonded to the C-terminus of SEQ ID NO:2 of the instant application):



ALMAGCIQEARERWNFDFVTETPLEGDFAWER

This qualifies as a "p21 carrier" and is excluded by the claims. But consider each of the following:

- 1 ALMXGCIQEARERWNFDFVTETPLEGDFAWER
- 2 ALMAGCINEARERWNFDFVTETPLEGDFAWER
- 3 ALMAGCIQEARERWNXDFVTETPLEGDFAWER
- 4 ALMAGCIQEARERWNFDLFTETPLEGDFAWER

In the first of these four sequences, "X" represents ethylglycine. The peptide chemist of ordinary skill would have expected that a peptide containing an alanine at a given position will exhibit substantially the same activity as an otherwise identical peptide containing ethylglycine [*In re Shetty* (195 USPQ 753); *In re Hass & Susie* (60 USPQ 544)]. At the same time, this sequence would qualify as a "non-p21 carrier". Consider next the second of the four sequences. In this case, the glutamine has been replaced with asparagine. Again, this would qualify as a "non-p21 carrier". Similar to the foregoing, in the third sequence, a phenethylglycine replaces phenylalanine, and in the fourth, a leucine replaces a valine. Thus, there are a number of peptides which are rendered obvious by Xiong, but which, at the same time, meet the requirement for a "non-p21 carrier".

In response to the foregoing, applicants have argued that the claims mandate that the "substance" contain no more than 40 amino acids. However, this assertion is factually incorrect. Next, applicants have argued the a reference is deficient unless it describes which fragments of p21 can inhibit a G1 Cdk. Perhaps if claim 1 actually mandated that the "substance" consist of 40 amino acids or less, applicants' argument would have some merit. But there is no such limitation.

Next, applicants have argued that Harper discloses that a peptide which consists of amino acids 1-60 of p21 is inactive in all assays. However, this is not what the reference teaches. Harper discloses (page 391) that a peptide consisting of amino acids 1-60 of p21 exhibits only minimal inhibition of cyclin A/Cdk2 when histone H1 was used as a substrate. This is quite different from saying that the peptide in question (1-60 of p21) is ineffective to inhibit all G1 cdk's in all assays. Furthermore, even if it were true that the peptide in question (1-60 of p21) is inactive in all assays of G1 cdk activity, the rejection would still be valid. As it happens, the claims encompass the possibility that the peptide fragment be coupled to a carrier; the claims require only that the "substance" exhibit activity, not that the "peptide fragment" exhibit any activity.

The rejection is maintained.



Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §103 as being unpatentable over Lin (*Mol Cell Biol* 16, 1786, 1996).

As indicated previously, Lin discloses inhibition of cdk's by p21; also disclosed, however, is inhibition of cdk's by peptides which are mutants of p21.

As such, the limitation of a "non-p21 sequence" is met by the reference.

In response, applicants have simply asserted that a given peptide which contains "n" amino acids is somehow different from a conjugate of a "first" peptide and "second" peptide, wherein the "first" peptide consists of "m" amino acids, and the "second" peptide consists of "n-m" amino acids. Thus, for example, according to applicants, if one were to take the peptide YGRTV and couple it to the peptide SQWPN to form the peptide YGRTVSQWPN the peptide formed in this way is somehow different from simply removing the peptide YGRTVSQWPN from a vial. Applicants, however, are incorrect both as a chemical matter and a legal matter. Unless applicants can point to some chemical or physical difference between a peptide that has been synthesized by coupling together two smaller peptides, and a peptide that has been made some other way (e.g., recombinantly or by stepwise peptide synthesis), applicants' position has no merit.

The rejection is maintained.



Claims 1-5, 8, 11, 12 are rejected under 35 U.S.C. §103 as being unpatentable over Toyoshima, (*Cell* 78, 67-74, 1994).

As indicated previously, Toyoshima discloses inhibition of cdk's by p27. Also as noted previously, the term "fragment" in instant claim 1 could mean just one single amino acid; thus, any amino acid that is present in p21 would qualify. As such, nearly any peptide that inhibits a G1 cdk would be encompassed by the claims. In addition, claim 3 is actually much broader in scope than claim 1; one can begin with a fragment of p21, select an "active portion" of that, and then make a derivative of the "active portion". As such, few peptides are excluded by claim 3.

In response, applicants have argued that the claims require the presence of the sequence KxxRRyFzP. As explained above in the rejection over Nakanishi, the claims do not actually require this.

The rejection is maintained.

✦

On page 5 of the response filed 4/25/07, applicants have argued that they have submitted a copy of each of several references. However, no such copies have been received. Accordingly, all references cited have been stricken from the IDS.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read 'D. Lukton', is positioned above the printed name.

DAVID LUKTON, PH.D.  
PRIMARY EXAMINER